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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,405	08/21/2000	Michael P. Neeper	20413Y	8029

7590 02/07/2005  
Alysia A. Finnegan  
c/o Merck & Co., Inc. Patent Dept.  
Ry60-30  
P.O. Box 2000  
Rahway, NJ 07065-0907

EXAMINER

LI, QIAN JANICE

ART UNIT PAPER NUMBER

1632

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	<b>Application No.</b> 09/642,405	<b>Applicant(s)</b> NEEPER ET AL.	
	<b>Examiner</b> Q. Janice Li	<b>Art Unit</b> 1632	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 27 December 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 27 December 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): Objections of claims 3 and 23.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: Z.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

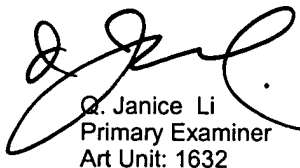
Claim(s) allowed: 11, 15 and 18.

Claim(s) objected to: Z.

Claim(s) rejected: 1-4, 6, 10, 17, 19-23, 31.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

  
 Q. Janice Li  
 Primary Examiner  
 Art Unit: 1632

Continuation of 5. does NOT place the application in condition for allowance because: Concerning the request for removal of finality of the previous Office action:

Applicants requested the Office to remove the imposition of finality of the previous Office action because the ground of rejection stating the claims are enabled for "codons optimized for expression in human 293 cells", but not "in any cell of a human host" was presented for the first time in the 9/22/04 action, which was not necessitated by Applicants' amendment or IDS.

In response, the issue was raised because of the Declaration of William L. McClements submitted 6/10/04, which is a form of information disclosure newly presented by the applicants. In point 6 of the declaration, Dr. McClements stated under oath, "Codon-optimization is not always successful at producing increased gene expression in a CELL TYPE of interest, and is not predictable of future success with a different virus". Thus, it is not premature to make the action final. Since the opinion is not based on the personal knowledge of the Examiner, but a skilled in the relevant art, it is not necessary to provide an Examiner's affidavit.

However, upon reconsideration, this rejection has now been modified to remove the scope limitation of human 293 cells, thus claim now is only limited to any human cells, which is consistent with the teaching of the specification and applicants argument. Such rejection is particularly relevant to claim 31, wherein the claimed process encompasses a host cell of any animal. For reasons set forth above, it is proper to maintain the finality.

Concerning rejections under 35 USC § 112, 1st paragraph:

Applicant first asserts, the Office concedes, "the claimed genus of codons could be made by the teaching of the specification". This is an inaccurate characterization of the merit of the Office action. The full citation of the Office action reads,

"THEORETICALLY the claimed genus of codons could be made by the teaching of the specification. However, in the response and Declaration of William L. McClements, the co-applicant and a skilled artisan cited numerous art of record and spoke from his own experience, stated that at the time of the invention, codon-optimization is not always successful at increasing expression of a particular gene, and successful condon-optimization of one gene is not predictive of the future success of a different gene. "We did not have an expectation of success" (point 5 of the Declaration). The declaration exemplified such opinion by a showing that the gene expression did not improve for the "optimized" HSV2 codon, and gene expression even decreased upon codon-optimization for tuberculosis. The declaration further indicated that the codon-optimization is not always successful at producing increased gene expression in a cell type of interest, and is not predictable of future success from one gene to the other (point 6 of the declaration). The declaration additionally indicated the presence of inhibitory sequences is unique for different genes (point 7 of the declaration). In view of such, what is successful for increased gene expression of HPV16 L1 gene is not predictable of the future success for HPV16 L2 gene, and likewise what is successful in 293 cells is not predictive of other human cell types".

Here, it is important to have "theoretically" being included in the citation, and to read the action as a whole.

Applicants then attempt to deny the full contents of the cited phrase in the declaration, acknowledging the unpredictability between viruses by highlighting the terms. However, it is apparent, the cited sentence first acknowledged the unpredictability of gene expression optimization (i.e. resulting in an increased gene expression by codon modification) for a given gene in a given cell type, and then the unpredictability from one virus to another virus. Applicants are further reminded that the differences among viruses are also a reflection of differences between the genes, because it is the difference in genetics among different viruses that determined the unpredictability of condon-optimization among different viruses.

Applicants request the Examiner points to specific lines where "the presence of inhibitory sequences is unique for different genes". In response, Applicants' attention is directed to lines 4-8 of point 7, wherein the two cis-acting inhibitory sequences identified in HPV16 L2 gene were not found in HPV1 L1 or L2 genes. Here again, the finding reflects that the L2 gene is different between HPV1 and HPV16, as much as the difference between the two viruses.

Accordingly, for reasons of record and set forth supra, the rejection stands.